Bevacizumab in Combination with Chemotherapy or Molecularly Targeted Agents for Non–Small-Cell Lung Cancer with Brain Metastases

To the Editor:

Su and Rau[1] have recently reported a case of non–small-cell lung cancer (NSCLC) of great interest. The patient, with anaplastic lymphoma kinase (ALK)-positive adenocarcinoma of the lung with brain metastases, was initially treated with whole-brain irradiation and then treated with chemotherapy consisting of pemetrexed and cisplatin; however, her brain metastases increased in size accompanied by muscle weakness and myoclonic jerks after two cycles of chemotherapy. The authors then added bevacizumab to the same chemotherapy and the brain metastases markedly shrank.

To date, it has been prospectively demonstrated that bevacizumab is safe and effective in NSCLC patients with brain metastases as long as these metastases are pretreated[2] or asymptomatic.[3] Moreover, a case series has shown that bevacizumab is also safe and effective for NSCLC patients with symptomatic, heavily pretreated brain metastases.[4] We also experienced a case of lung adenocarcinoma in which the brain metastases were refractory to whole-brain irradiation but dramatically responded to combination chemotherapy of bevacizumab, paclitaxel, and carboplatin (Fig. 1). These findings suggest that bevacizumab may merit further investigation in NSCLC patients with symptomatic, heavily pretreated, and/or radioresistant brain metastases.

In addition, a recent retrospective study demonstrated that brain metastases are considerably common at the time of diagnosis and also at the time of disease progression in epidermal growth factor receptor (EGFR)-positive or ALK-positive NSCLC treated with tyrosine kinase inhibitors (TKIs).[5] Considering that bevacizumab may have some booster effect for brain metastases and that brain metastases have a negative impact on survival in EGFR-positive NSCLC treated with EGFR-TKI as well,[6] prospective evaluation of bevacizumab in combination with TKI in EGFR-positive or ALK-positive NSCLC patients with brain metastases would be particularly valuable.

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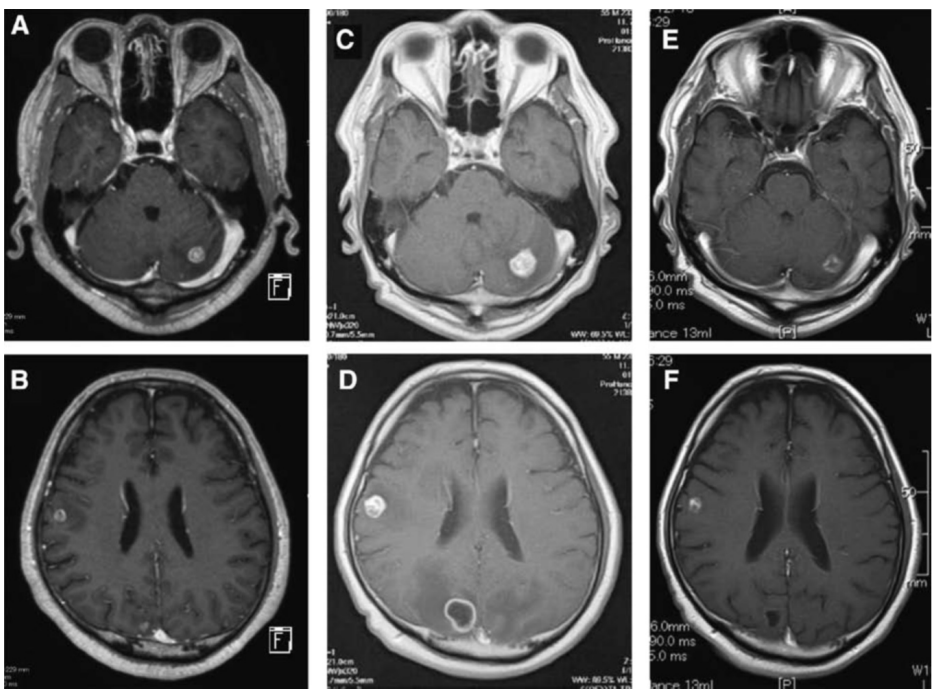

FIGURE 1. Magnetic resonance imaging of the brain (*A*,*B*) before and (*C*,*D*) after whole brain irradiation, (*E*,*F*) after two cycles of chemotherapy of bevacizumab, paclitaxel, and carboplatin.